Amendments to the Drawings:

The attached sheets of drawings include changes to Figs. 1, 4 and 5. The sheets, which include Figs 1, 4 and 5, replace the originally filed sheet.

Attachment: Replacement Sheets

REMARKS

The Office Action of October 31, 2005 has been carefully considered. Claim 1 is amended and new claim 21 is added. Support for new claims 21-23 is found throughout the specification and particularly at page 7, lines 6-19. Claims 1-11 and 21-23 are currently pending.

Drawings

The Office Action indicates that Figures 1, 2, 4, 5, and 6 are objected to and should be designated as –Prior Art--. In response, the replacement Figures 1, 4, and 5 are submitted herewith in compliance with the Office Action. The objection to Figures 2 and 6 is traversed.

Figure 2 is clearly not prior art and the specification does not describe it as such. See for example the Specification at page 8, lines 1-5 and the Specification at page 10 lines 2-4 which states, "FIG. 2 shows this preferred example labeled substrate for use in the substrate displacement assays of the present invention." Likewise, Figure 6 is also not prior art. Figure 6 displays a fluorescence anisotropy curve for F1 as function of MurG concentration. Removal of the objection to these figures is requested.

Claim Rejections – 35 USC § 103

Claims 1 – 11 are rejected under 35 USC § 103(a) as being unpatentable over Branstrom et al. (2000) in view of Helm et al. (2002) and Lazar et al. (2002). This rejection is traversed.

As indicated in the Office Action, Branstrom et al. does not teach the measurement of labeled substrate bout to the glycotransferase, the use of the method to identify a compound that specifically inhibits the ability of a glycotransferase to bind a substrate, the use of fluorophore fluroscein, or a labeled substrate which is UDP-GlcNac analogue. In short Branstrom et al. does not teach or suggest a number of required elements of the pending claims. These elements absent in Branstrom et al. are not provided by or suggested in the disclosure of Helm et al. or Lazar et al.

Branstrom et al. and Helm et al. both disclose and are directed to kinetic assays, while in contrast, the invention as currently claimed is based on a donor displacement assay. Helm et al. describes substrate analogs used to assay MurG; the assays however are kinetic assays, which are

completely different from the donor displacement assays and do not enable facile, high throughput screening (identification). Furthermore, the substrate analogs used are acceptor analogs, as opposed to the method as currently claimed in which donor analogs are used.

The differences between a kinetic assay and a displacement assay, and additionally between the donor and acceptor substrates, are quite significant and are not interchangeable to those skilled in the art. A kinetic assay to screen for inhibitors of MurG is different for several reasons. For one reason, the Lipid I substrate analogue used to assay the enzyme is prepared by a long and difficult chemical synthesis, and a random screen requires using large amounts of this compound. In addition, kinetic assays also require precise timing and can be technically demanding, particularly if they involve secondary enzymes to detect product, as a colorimetric assay does. Finally, kinetic assays are often subject to nonspecific inhibition by compound aggregates, which creates uncertainty of the results obtained.

In contrast, the current invention as claimed in Claims 1-11 and claim 21 recite an assay that utilizes a donor displacement assay. In addition to being straightforward, technically simple, and inexpensive, a donor displacement assay provides other advantages that make it particular useful for the screening of compounds. For one example, because the assay is based on displacement of a ligand from the glycosyl donor binding site, a relatively high number of hits bind to a single region of the enzyme. As a result, the structural requirements for binding to that region of the enzyme emerge quickly from an analysis of the data. In contrast, kinetic assays yield compounds that operate by a number of different mechanisms, making structure-activity relationships more difficult to analyze. Additionally, the method provides fewer false positives related to compound aggregation in the displacement assay compared with a kinetic assay due to reduced sensitivity to artifacts related to compound aggregation. Finally, the donor displacement assay can be readily adapted to screen any glycosyltransferase, for example, in which at least one modifiable group on the nucleotide-sugar is solvent exposed. See Specification at page 11, lines 12-15.

For these reasons, the Applicants submit that one skilled in the art could not combine the teachings of Branstrom et al., and Helm et al. and Lazar et al. to produce the method of as currently claimed. One of ordinary skill in the art would not simply decide to substitute the

donor displacement assay of the current invention with the kinetic assay of Helm et al. and Branstrom et al. with any expectation of success. To suggest that the substitution is obvious is to engage in impermissible hindsight since there is no suggestion in either of the references that such a substitution is even possible. Therefore, the Applicants submit the invention is not obvious.

In view of the foregoing, Applicants submit that all pending claims are in condition for allowance and request that all claims be allowed. The Examiner is invited to contact the undersigned should he believe that this would expedite prosecution of this application. It is believed that no fee is required. The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,

Dated: April 20, 2006

Christopher S. Casieri
Reg. No. 50,919
Attorney for Applicant

MATHEWS, SHEPHERD, McKAY & BRUNEAU, P.A.
100 Thanet Circle, Suite 306
Princeton, NJ 08540
Tel: 609 924 8555
Fax: 609 924 3036